Pediatr Neonatol 2008;49(2):43–47

CASE REPORT

Hydranencephaly Associated with Interruption of Bilateral Internal Carotid Arteries

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Received: Aug 30, 2007
Revised: Jan 26, 2008
Accepted: Mar 25, 2008

KEY WORDS:
hydranencephaly;
hydrocephalus;
magnetic resonance angiography;
magnetic resonance imaging;
sonography

Hydranencephaly is a rare and fatal central nervous system disorder where all or nearly all of the bilateral cerebral hemispheres are absent. The extensive hollow cerebrum is replaced with cerebrospinal fluid. Clinically, the differential diagnoses of hydranencephaly include severe hydrocephalus and alobar holoprosencephaly. Nearly all cases are sporadic, involving approximately 1 in 5000 continuing pregnancies. The exact main cause is still unknown, but hydranencephaly is usually found to develop secondarily to the occlusion of cerebral arteries above the supraclinoid level. We present the case of a 1-month-old male infant with hydranencephaly initially thought to be severely hydrocephalus via routine antenatal intrauterine sonography performed at 35 weeks of gestation. Hydranencephaly was confirmed by brain sonography, brain magnetic resonance imaging and magnetic resonance angiography postnatally. We discuss several imaging features that are helpful in distinguishing hydranencephaly from extreme hydrocephaly. Different theories that have been recently proposed regarding the origin of hydranencephaly are reviewed.

1. Introduction

Hydranencephaly is a rare and fatal central nervous system disorder where all or nearly all of the bilateral cerebral hemispheres are absent. The extensive hollow cerebrum is replaced with cerebrospinal fluid and debris covered with a thin, membranous, cerebrospinal fluid-filled sac. Small portions of the frontal lobe, temporal lobe and most of the occipital lobe may be preserved; moreover, the basal ganglia and the thalami may reveal hypoplasia, whereas the brainstem and cerebellum are usually present and intact. It has been reported in 0.2% of infant autopsies.[1] Hydranencephaly often occurs as an isolated defect without other associated malformations. Nearly all cases are sporadic, involving approximately 1 in 5000 continuing pregnancies.[2,3] Hydranencephaly was first described by Cruveilhier in 1835. Several theories on the pathogeneses of hydranencephaly have been proposed over the last

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180 years. Etiologies are associated with infectious, toxic, aplastic, genetic, or vascular origin, maternal hypoxia or fetofetal transfusion syndrome. The exact main cause is still unknown, but hydranencephaly is usually found to develop secondarily to the occlusion of cerebral arteries above the supraclinoid level, mostly affecting the major vessels of the anterior circulation.[4] Here, we report the case of a male infant with hydranencephaly confirmed by magnetic resonance angiography (MRA).

2. Case Report

The patient was a full-term male infant born to a 38-year-old mother at the gestational age of 38 weeks via Cesarean section due to breech presentation. Apgar score was 7 at 1 minute and 8 at 5 minutes. His birth body weight was 2750 g (appropriate for gestational age), his body length was 47 cm (10th percentile), and his head circumference was 42 cm (>95th percentile). There were no immediate postnatal insults. No prenatal survey was sought until 35 weeks of gestation. Fetal ultrasonography revealed hydrocephalus. The mother did not undergo further examination. Maternal history was unremarkable. No known teratogenic or infectious exposures were documented during pregnancy. Two other children previously born to this mother were physically healthy.

The general physical findings of this newborn were unremarkable. The anterior fontanelle was full and soft but not bulging, measuring about 3×3 cm in size; no sunset eyes were found. On neurologic examination, light reflex of bilateral eyes was faint, while sucking and swallowing ability were fair, generalized muscle tone was mildly decreased, and Moro and sucking reflexes were positive. Emotional irritability with high pitched cry was noted under stimulation. Electroencephalography revealed low amplitude ($<25\,\mu v$), slow wave and poor modulation with no background. Both visual evoked potentials and brainstem auditory evoked potential tests showed non pick-up. Karyotype was a normal 46XY. Significant diffuse transillumination of the scalp was found when a Welch Allyn lite pipe neonatal transilluminator was applied to the anterior and posterior fontanelles (Figure 1).

Brain ultrasonography showed absence of bilateral cerebral hemispheres but intact cerebellar vermis. Subsequent brain magnetic resonance imaging (MRI) and MRA revealed nearly total parenchymal loss of the entire forebrain with brain tissue replaced by cerebrospinal fluid, except for small right inferior medial temporal lobes, small bilateral medial occipital lobes, and small thalami, suggesting hydranencephaly (Figures 2A, 2B, 2C). The falx cerebri

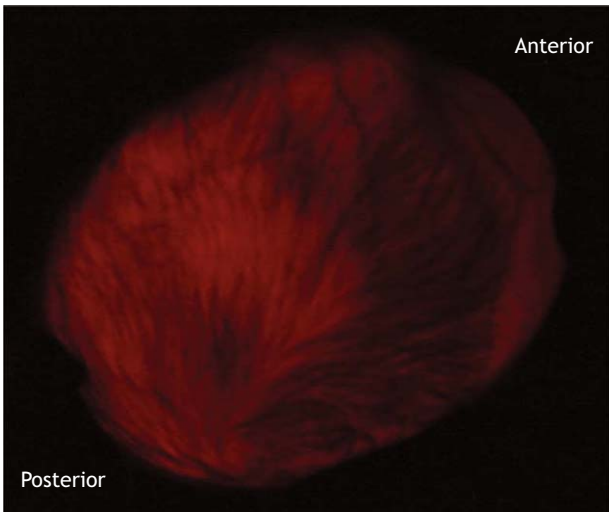

Figure 1 Significant diffuse transillumination of the scalp was found when using a Welch Allyn lite pipe neonatal transilluminator applied to the posterior fontanelle.

was well demonstrated, but atrophy of the midbrain and mild atrophy of the hindbrain were noted. Bilateral vertebral arteries were well developed, but development of the branches of the basilar artery and bilateral intracranial internal carotid arteries (ICAs) was interrupted at the level of C4 (Figure 3). Short T1 signal focus was strong in the sella turcica, suggesting at least some development of the pituitary gland (Figure 2D).

Magnetic resonance phase contrast flow images showed increased resistance of bilateral common carotid arteries; the resistive index of the right common carotid artery (CCA) was $(16.1-0)/16.1=1.0$, and that of the left CCA was $(27.1-3.0)/27.1=0.89$ (normal range, 0.5–0.8), compatible with distal occlusion (Figure 4). The bilateral ICAs were short and severely hypoplastic, so the resistive index could not be measured. At 16 weeks of age, the head circumference was 59 cm. Vital signs were stable since the first day of admission. Blood culture, cerebral spinal fluid culture and TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes simplex) survey were unremarkable. Progressive enlargement of the skull made oral feeding with the head tilted up difficult. Thus, feeding via nasogastric tube was begun. Feeding was advanced to 85 mL every 3 hours.

3. Discussion

Clinically, differentiating hydranencephaly from other cystic lesions, such as severe hydrocephalus and alobar holoprosencephaly, is always challenging. Sonographically, there is no uniform rim of cortical remnant noted in hydranencephaly. However, about 1% of infants thought to have hydrocephalus

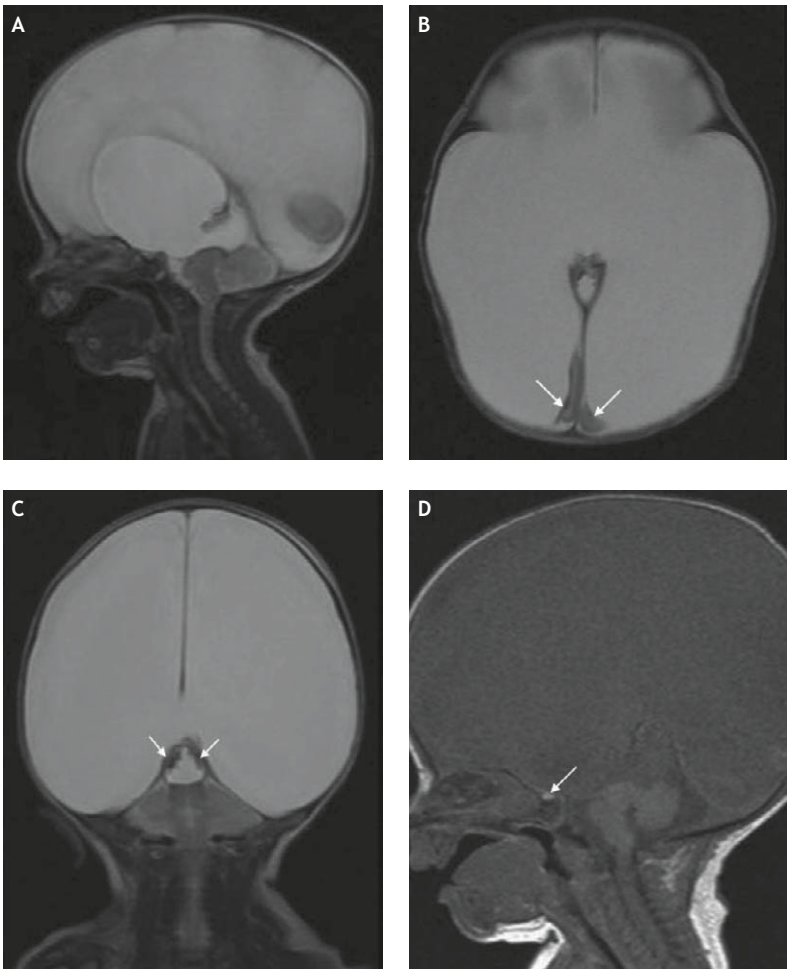

Figure 2 (A) Sagittal T2-weighted image of the brain demonstrates the falx cerebri and cerebellum. A small remnant of occipital lobe is shown. Atrophy of the midbrain and mild atrophy of the hindbrain are noted. (B) Axial T2-weighted image of the brain shows that only a small portion of bilateral medial occipital lobes remain (arrows). It can be seen that there is nearly total parenchymal loss of the entire forebrain, with brain tissue replaced by cerebral spinal fluid. (C) Coronal T2-weighted image of the brain. The falx cerebri is present, and the thalami are hypoplastic and poorly lobulated (arrows). (D) Sagittal T1-weighted image of the brain, with good demonstration of short T1 signal focus in the sella turcica, suggesting at least somewhat poor development of the pituitary gland (arrow).

are later found to have hydranencephaly.[5] The two conditions can be differentiated by further neuroimaging with angiography and, at autopsy, by considering the morphology of the ICAs. Hydranencephaly is found to be related to bilateral ICA occlusion, whereas the terminus of ICAs are splayed and distorted but still remain in hydrocephalus.[6] Bilateral ICA occlusion is generally considered the specific angiographic hallmark of hydranencephaly, which helps to differentiate it from severe hydrocephalus. On the other hand, alobar holoprosencephaly is characterized by the presence of a fused thalamus, a single horseshoe-shaped ventricle, a pancake-shaped mass of fused frontal-lobe tissue and absence of cerebral falx and corpus callosum. Hydranencephaly can usually be differentiated from alobar holoprosencephaly by the appearance of the cerebral falx and lobulated thalami. Thus, angiographic imaging plays an important role in arriving at a definite diagnosis of hydranencephaly. Jordan et al[6] and Hochmuth and Wentz[7] reported cases of hydranencephaly with more well-developed vascular distribution than our case. The case reported by Jordan et al was found to have patent proximal portion of the bilateral anterior cerebral arteries (ACAs) and posterior cerebral arteries (PCAs). The patent portion of the ACAs divides into several cortical branches. Although the bilateral middle cerebral arteries (MCAs) were hypoplastic, they were found to have vascularized a small island of residual brain tissue on each side.[6] Similarly, the case presented by Hochmuth and Wentz[7] demonstrated well-developed bilateral posterior communicating arteries but hypoplastic ACAs, MCAs and PCAs. By comparison, in our case, MRA revealed interruptions of the bilateral intracranial ICAs and of the branches of the basilar

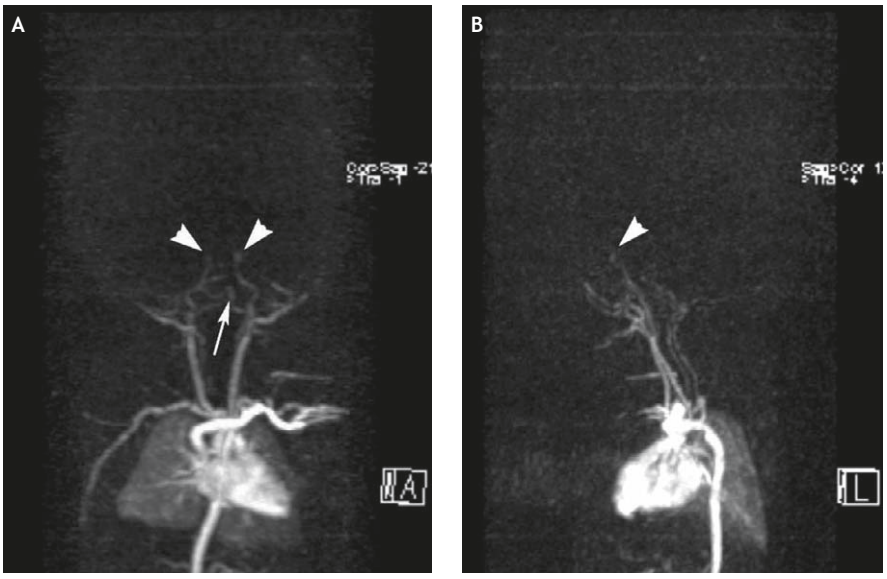

Figure 3 (A) Magnetic resonance angiography (MRA), anterior view, shows interruption of bilateral intracranial internal carotid arteries (ICAs) (arrowheads) and good demonstration of bilateral vertebral arteries but interruption of branches of the basilar artery (arrow). (B) MRA, lateral view: bilateral cavernous (juxtasellar) ICA was found interrupted at the C4 or posterior genu segment (arrowhead).

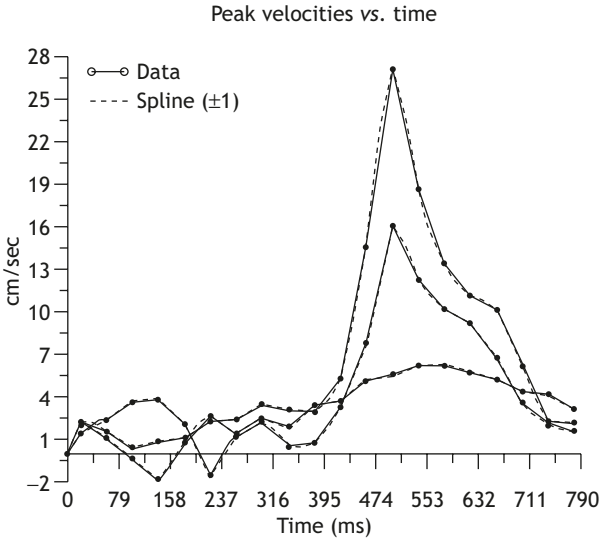

Figure 4 Magnetic resonance phase contrast flow images show increased resistivities of bilateral common carotid arteries (CCAs), compatible with distal occlusion. Resistive index of right CCA=(16.1−0)/16.1=1.0. Resistive index of left CCA=(27.1−3.0)/27.1=0.89 (normal range, 0.5–0.8).

artery. The branches of the bilateral ICAs, bilateral ACAs, MCAs and PCAs were all absent (Figure 3). Most of the territories dependent on vertebrobasilar circulation—including the right inferior medial temporal lobes, the bilateral medial occipital lobes, and the thalami—were present but in a rather smaller size. This is compatible with the findings reported in previous studies.

On the other hand, not all cases of hydranencephaly present with complete occlusion of bilateral ICAs or vertebrobasilar vessels. La Torre and Occhipinti[8] reported three cases of hydranencephaly whose angiographic studies showed both ACAs and MCAs present but stretched "as in the extreme degree of hydrocephalus". The case reported by Jordan et al was found to have a vascular variant with a hypertrophied anterior choroidal artery which vascularized the PCA territory. Moreover, a small island of residual cerebral tissue was detected in the middle cranial fossa which was supplied by an atrophic remnant of the left MCA.[2]

Several pathogeneses have been proposed recently for this condition. Fetal encephalitis caused by certain viral infections may be a possible origin of hydranencephaly. A study from Israel found that Akabane virus (AKAV) and Aino virus (AINV) could cause teratogenic malformations when they infected immunologically naive pregnant ruminants.[9] In pregnant cows, the virus can invade the fetus, where it infects the central nervous system or skeletal muscle tissues, and so causes hydranencephaly/hydrocephaly/microencephaly (HE/ME) and encephalomyelitis or arthrogryposis.[7] AKAV belongs to the Simbu serogroup of the arthropod-borne genus *Orthobunyavirus* of the family *Bunyaviridae*. AKAV is transmitted by blood-sucking insects, such as biting midges and mosquitoes.[9] However, to the best of our knowledge, neither AKAV nor AINV infection in humans has been reported. A study from Germany reported a case of triplets with fetofetal transfusion syndrome in which two fetuses developed

hydranencephaly and the third was a fetus papyraceus. The histopathology of hydranencephaly is characterized by massive necrosis, macrophage invasion and endothelial proliferation. Multiple arteriovenous anastomoses were found in the monochorial triamniotic placenta and multiple organ infarction was detected in one of the fetuses, suggesting that various mechanisms causing thromboembolic events in the fetus may be attributed to the pathogenesis of hydranencephaly.[10] Moreover, Halsey et al found that hydranencephaly could be created *in utero* in monkeys through ligation of the jugular vein.[11]

Infants with hydranencephaly raise medical, ethical and legal issues for further discussion. A definite diagnosis of hydranencephaly is crucial for parents to understand fully, before they decide on further medical treatment that may prolong survival but not influence the neurodevelopmental outcome. Previous studies proposed that hypothalamic-pituitary-adrenal function is essential for prolonged survival.[12] The thalamic circuits play an important role in consciousness, but no improvement in consciousness or awareness was found even in patients with intact thalamic circuits.[4] Although the literature documents rare cases of prolonged survival up to 19 years, prognosis is extremely poor, with severe neurologic dysfunction, seizures, myoclonus, respiratory failure and death usually progressing within the first few days or weeks of life.[5] Thus, it is crucial for pediatricians to counsel parents carefully, to prevent the family from having any false hopes with regard to the outcome of the disease.

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